

REMARKS

Claims 25-30 and 36 are pending in this application. Applicants have amended claim 25. Support for the amendments can be found, for example, at page 42, second full paragraph and page 54, first paragraph. No new matter has been added.

Withdrawn Rejections

Applicants thank the Examiner for withdrawing the previously-raised 35 U.S.C. § 102 rejection based on Deghenghi (U.S. Pat. No. 5,962,409).

35 U.S.C. § 102

Smith et al. (Endocrine Reviews 18:621-645 (1997))

The Office (at pages 4-7 of the Office Action) maintains its rejection of claims 25-30 and 36 as allegedly being anticipated by Smith et al. (“Smith”).

Applicants respectfully disagree with the Office’s position. In addition to the following remarks, Applicants re-iterate the remarks filed in their previous Replies.

In part, the Office alleges at page 5, “Smith et al, throughout the publication, teach various compounds (peptidomimetics) that can be used for regulation of growth hormone (GH) secretion (see entire document).”

However, the compounds described in Smith are not direct antagonists of GH secretion. As stated in the sentence bridging pages 622-623 of Smith, “approximately 120 compounds were selected for their ability to stimulate GH release.” Thus, as these compounds stimulate GH release, these compounds in Smith are not direct antagonists of the GH/IGF-1 axis.

Further, the method of amended claim 25 includes the steps of (a) providing a small molecule that is obtained by chemically modifying an agonist of a GH/IGF-1 axis component selected from the group consisting of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, and Akt-3 while retaining a structure of the agonist that is capable of a physical aspect of the interaction of the agonist with the component or that is selected for structural similarity to an agonist of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3; and (c) identifying the small molecule as a GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 antagonist wherein the small molecule antagonizes the activity of

GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3, thereby providing a GH/IGF-1 axis direct antagonist.

Smith fails to teach these steps, and thus fails to anticipate claim 25 and its dependencies.

Further, Applicants note that the Office at page 7, first paragraph, alleges that:

In addition, the instant application also seems to define the term 'antagonist' as acting positively on the GH-IGF-1 components. For example, the instant disclosure states, 'The agent can be ... a direct antagonist, e.g., of a positively acting component of the GH/IGF-1 axis.' (spec., p.5, para. 2). That is an antagonist can 'positively' act on or activate the GH/IGF-1 components.

Applicants respectfully point out that the Office has mischaracterized a disclosure of the application. A direct antagonist of a positively acting component of the GH/IGF-1 axis reduces the activity of the positively-acting component; this is not the same as acting 'positively' on the GH/IGF-1 axis, as the Office misconstrues. For further understanding, see, for example, page 49, and Table 1. As indicated at page 49:

There are a variety of methods that can be used to down regulate the GH/IGF-1 axis. For example, axis activity can be reduced by targeting a particular component of the axis. Depending on the component's function in the axis, it may be appropriate to inhibit its activity or to promote its activity. For example, axis activity can be reduced by agonizing an inhibitory component of the axis or antagonizing a component that promotes or is required for axis activity. Exemplary targets and the desired activity used against these targets to reduce axis activity are listed in Table 1.

MK-0677, which the Office states has the "ability to increase GH release (i.e. positively acting)" (Office Action at page 7) is not an antagonist of the GH/IGF-1 axis.

In summary, Smith fails to teach a method of identifying a GH/IGF-1 axis direct antagonist, not to mention a method that includes the steps recited in claim 25. For at least these reasons, Applicants respectfully request that the § 102 rejection of claims 25-30 and 36 based on Smith be withdrawn.

35 U.S.C. §§ 102 and 103

Blum et al. (Biochemistry 39:15705-15712 (2000))

The Office at pages 8-11 of the Office Action alleges that claims 25, 26, and 36 are anticipated by, or obvious in light of, Blum et al. ("Blum").

Applicants respectfully disagree with the Office's position. In addition to the following remarks, Applicants re-iterate the remarks filed in their previous Replies. The method of amended claim 25 recites, in part, the steps of (a) providing a small molecule that is obtained by

chemically modifying an agonist of a GH/IGF-1 axis component selected from the group consisting of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, and Akt-3 while retaining a structure of the agonist that is capable of a physical aspect of the interaction of the agonist with the component or that is selected for structural similarity to an agonist of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3; and (c) identifying the small molecule as a GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 antagonist wherein the small molecule antagonizes the activity of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3, thereby providing a GH/IGF-1 axis direct antagonist.

As Blum fails to teach these steps, it fails to anticipate claims 25, 26 and 36 or render them obvious.

Further, Applicants note that the Office at page 10 alleges that:

In addition, the IGF-1 receptor kinase inhibitors of the Blum reference are structurally similar to the substrate (or ligand, or an agonist) of the IGF-1 receptor kinase (i.e. a tyrosine residue), and thus would be a chemical modification of the compound, tyrosine, or an agonist.

Applicants respectfully disagree with the Office's position. The IGF-1 receptor acts on a receptor substrate. A substrate of the IGF-1 receptor is not the same thing as an agonist of the receptor. The Office has not provided any support for its allegation that a substrate (specifically, the tyrosine residues) of the IGF-1 receptor is an agonist of the receptor. Thus, for this additional reason, Blum fails to teach, or render obvious, the method of claim 25.

For at least these reasons, Applicants respectfully request that the §§ 102 and 103 rejections of claims 25, 26, and 36 based on Blum be withdrawn.

Orrego et al. (J. Clin. Endocrinol Metab. 86:5485-5490 (2001))

The Office alleges that claims 25-30 and 36 are anticipated by, or obvious in light of, Orrego et al. ("Orrego") (pages 11-15 of the Office Action).

Applicants respectfully disagree with the Office's position. In addition to the following remarks, Applicants re-iterate the remarks filed in their previous Replies. The method of amended claim 25 recites, in part, the steps of (a) providing a small molecule that is obtained by chemically modifying an agonist of a GH/IGF-1 axis component selected from the group

consisting of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, and Akt-3 while retaining a structure of the agonist that is capable of a physical aspect of the interaction of the agonist with the component or that is selected for structural similarity to an agonist of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3; and (c) identifying the small molecule as a GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 antagonist wherein the small molecule antagonizes the activity of GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3, thereby providing a GH/IGF-1 axis direct antagonist.

Because Orrego fails to teach or suggest, *inter alia*, these steps, it does not anticipate or render obvious claim 25 and its dependencies.

Further, Applicants note that the Office alleges at page 14:

Applicants also assert that Orrego “fails to disclose evaluating activity of a GH/IGF-1 activator in the presence of a small molecule ...” (emphasis added; Reply, p.10, para. 3). Applicants seems to assert the reference does not teach evaluating an additional “activator” in the presence of the agonist. However, this is not a feature recited in the instant claim ... [et seq.]

Applicants respectfully point out that the Office has mischaracterized the claims and the content of the previously-filed Reply. As stated in footnote 1 on page 7 of the previously-filed Reply:

¹ Solely to reduce the length of the description of a term in claim 25, in this response, the term “GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3” has been abbreviated as “GH/IGF-1 axis activator”.

Thus, the Office’s remarks fail to point out any deficiencies of the previously-made remarks.

Because Orrego fails to teach, or even suggest, the steps recited in claim 25, Applicants respectfully request that the §§ 102 and 103 rejections of claims 25-30 and 36 based on this reference be withdrawn.

CONCLUSION

For at least the reasons stated above, Applicants respectfully submit that all pending claims are in condition for allowance, which action is expeditiously requested. Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do Applicants

concede that there are not other good reasons for patentability of the presented claims or other claims.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. Please charge any deficiency to Deposit Account No. 50/2762.

Respectfully submitted,
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Docket No.: E2023-701710

Date: December 5, 2008